Urgent carotid endarterectomy to prevent recurrence and improve neurologic outcome in mild-to-moderate acute neurologic events

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Objectives: **This study evaluated the safety and benefit of urgent carotid endarterectomy (CEA) in patients with carotid disease and an acute stable neurologic event.**

Methods: **The study involved patients with acute neurologic impairment, defined as ≥4 points on the National Institutes of Health Stroke Scale (NIHSS) evaluation related to a carotid stenosis ≥50% who underwent urgent CEA. Preoperative workup included neurologic assessment with the NIHSS on admission or immediately before surgery and at discharge, carotid duplex scanning, transcranial Doppler ultrasound imaging, and head computed tomography or magnetic resonance imaging. End points were perioperative (30-day) neurologic mortality, significant NIHSS score improvement or worsening (defined as a variation ≥4), and hemorrhagic or ischemic neurologic recurrence. Patients were evaluated according to their NIHSS score on admission (4-7 or ≥8), clinical and demographic characteristics, timing of surgery (before or after 6 hours), and presence of brain infarction on neuroimaging.**

Results: **Between January 2005 and December 2009, 62 CEAs were performed at a mean of 34.2 ± 50.2 hours (range, 2-280 hours) after the onset of symptoms. No neurologic mortality nor significant NIHSS score worsening was detected. The NIHSS score decreased in all but four patients, with no new ischemic lesions detected. The mean NIHSS score was 7.05 ± 3.41 on admission and 3.11 ± 3.62 at discharge in the entire group ($P < .01$). Patients with an NIHSS score of ≥8 on admission had a bigger score reduction than those with a lower NIHSS score (NIHSS 4-7; mean 4.95 ± 1.03 preoperatively vs 1.31 ± 1.7 postoperatively, NIHSS ≥8 10.32 ± 1.94 vs 4.03 ± 3.67; $P < .001$).**

Conclusions: **In patients with acute neurologic event, a high NIHSS score does not contraindicate early surgery. To date, guidelines recommend treatment of symptomatic carotid stenosis ≤2 weeks from onset of symptoms to minimize the neurologic recurrence. Our results suggest that minimizing the time for intervention not only reduces the risk of recurrence but can also improve neurologic outcome. (J Vasc Surg 2011;53:622-8.)**

The efficacy of carotid endarterectomy (CEA) in preventing stroke has been demonstrated in well-known large randomized prospective trials.[1,2] Subgroup analysis of those studies has defined some guidelines to treat recently neurologic symptomatic patients who have been monitored for many years. According to those studies, surgery had to be delayed for at least 6 weeks from the neurologic event because of the risk of hemorrhagic transformation of the acute brain ischemic lesion. Nevertheless, recent studies have emphasized the safety of early CEA in patients with nondisabling stroke or acute neurologic events.[3-7] Moreover, previous reports on early CEA[8,9] have shown that expedited carotid revascularization can improve neurologic outcome, as evaluated by the National Institutes of Health Stroke Scale (NIHSS), probably recruiting brain areas that can be reperfused before cell death occurs. The aim of this prospective study was to evaluate the safety and benefit of urgent CEA in a consecutive series of patients presenting with carotid disease and a mild or moderate acute stable neurologic event.

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METHODS

The intervention protocol reported in this article was approved by the Local Ethical Committee. All patients gave their written informed consent before CEA.

Patient population. From January 2005 to December 2009, all patients presenting to our Academic Emergency Department with neurologic symptoms were evaluated by a neurologist who established the initial neurologic severity and an NIHSS score. Onset time was recorded in all patients. When the onset of neurologic symptoms was unknown, it was considered as the last time the patient was seen free from symptoms.

All patients underwent a complete medical examination, NIHSS assessment, blood test, electrocardiogram, and cerebral computed tomography (CT) or magnetic resonance imaging (MRI) to assess the presence, nature, and extension of brain lesions. Carotid duplex ultrasound imaging and transcranial Doppler (TCD) imaging were performed in all patients to detect the eventual source of embolism. All patients received body-weight-adapted low-molecular-weight heparin (100 IU/kg twice daily), to-

Table I. Inclusion and exclusion criteria for patient enrollment

Inclusion criteria
Clear time of onset of symptoms
NIHSS score <22
Recent ischemic hemispheric brain infarct <33% of the middle cerebral artery area regardless of BBB disruption at CT or MRI scans
Internal carotid artery stenosis ≥70% or ≥50% with an ulcerated surface plaque at US evaluation
Patent middle cerebral artery in the detectable portion M1 and M2
Exclusion criteria
According to clinical presentation on admission
No clear time of onset of symptoms
Severe neurologic deficit (NHISS score >22)
Cerebral ischemia onset with seizures
Previous ischemic or hemorrhagic stroke with residual severe deficit (Modified Rankin Scale ≥2)
History of cerebral hematomas
Any other cerebral disease with residual permanent deficit
According to CT or MRI scans on admission
Recent ischemic hemispheric brain infarct >33% of the middle cerebral artery area
Presence of cerebral hemorrhage
Brain tumor
Cerebral arteriovenous malformation
Cerebral aneurysm

BBB, Blood brain barrier; *CT,* computed tomography; *MRI,* magnetic resonance imaging; *NIHSS,* National Institutes of Health Stroke Scale; *US,* ultrasound.

gether with their scheduled antihypertensive, statin, or antidiabetic medications. Blood pressure, temperature, and serum levels of glucose were strictly monitored.

In 113 of 1889 patients (6%) admitted to our Emergency Department Stroke Unit, an ipsilateral ≥50% carotid stenosis (North American Symptomatic Carotid Endarterectomy Trial evaluation criteria[2]) was encountered, and 62 (55%) were scheduled for urgent CEA, respecting inclusion and exclusion criteria and stabilization of symptoms at time of CEA (Table I).

The study excluded patients who received thrombolytic treatment with recombinant tissue plasminogen activator (rt-PA) and CEA (European Medicines Evaluation Agency Criteria, Safe Implementation of Thrombolysis in Stroke-Monitoring Study[10]). Patients who presented with unstable symptoms and underwent urgent CEA were excluded from the present analysis.

Perioperative management. CEA was performed under general anesthesia in all cases. Routine physiologic monitoring included pulse oximetry, electrocardiogram, and invasive blood pressure measurement using the radial artery. Before the internal carotid artery (ICA) was clamped, heparin (5000 ± 2000 IU, depending on body weight) was injected intravenously. Neurologic status assessment was performed using near-infrared spectroscopy (NIRS) in all cases and TCD imaging whenever possible throughout the entire procedure.

CEA was performed by standard surgical protocol in all cases. Dacron patch angioplasty was performed in 43 patients (69.4%) using 5-0 polypropylene suture in a semicontinuous fashion, and direct closure was made in 19 (30.6%) in a continuous fashion. A shunt was used in 13 patients (21%) when a >50% reduction in the middle cerebral artery mean velocity at TCD monitoring or a >20% reduction of regional oxygen saturation at NIRS monitoring was detected.

Table II. Analysis of clinical and demographic characteristics with respect to significant (≥4) postoperative National Institutes of Health Stroke Scale (*NIHSS*) score decrease[a]

Variable	*No. (%)*	*NIHSS score decrease ≥4* *No. (%)*	P
Patients, No.	62	28	
Age <70 years	22 (35.5)	12 (54.5)	.11
Age ≥70 years	40 (64.5)	16 (40)	
Male	51 (82.2)	24 (47)	.22
Hypertension	49 (79)	23 (46.9)	.21
Diabetes	21 (33.8)	9 (42.8)	.50
Hyperlipemia	19 (30.6)	9 (47.3)	.51
Smoke	37 (59.6)	20 (54)	.05
Coronary artery disease[b]	20 (32.2)	10 (50)	.18
Brain infarction on admission	36 (58)	16 (44.4)	.20
CEA ≤6 hours	22 (35.4)	10 (45.4)	.60
NIHSS score			
4-7 on admission	40 (64.5)	11 (27.5)	<.0001
≥8	22 (35.5)	17 (77.2)	
ICA stenosis			
50%-69%	22 (35.5)	11 (50)	.16
≥70%	40 (64.5)	16 (40)	
Plaque composition			
Hyperechoic	15 (24.2)	7 (46.6)	.56
Hypoanechoic	47 (75.8)	21 (44.7)	

CEA, Carotid endarterectomy; *ICA,* internal carotid artery.
[a]Categoric data analysis by Fisher's exact test.
[b]Includes myocardial infarction, angina, congestive heart failure, valvular heart disease.

In the postoperative period, patients were maintained under a low dosage of heparin (4000 IU enoxaparin sodium) together with their scheduled medications. Systolic blood pressure was maintained <140 mm Hg in the immediate postoperative period. Antiplatelet therapy with acetylsalicylic acid (100 mg daily) was started at discharge.

All patients were evaluated by an experienced neurologist (D.T.) immediately after surgery, at discharge, and at the 1-month follow-up with recording of any neurologic adverse event and an NIHSS score assessment. Postoperative neuroimaging was only performed in those patients presenting a worsening NIHSS score.

End points and statistical analysis. Patients were evaluated according to neurologic impairment assessed by the NIHSS score on admission or immediately before surgery (score 4-7, mild acute neurologic impairment; score ≥8, moderate acute neurologic impairment[11]), clinical and demographic characteristics (Tables II and III), timing of surgery (before or after 6 hours), and presence of brain infraction on neuroimaging.

Table III. Analysis of clinical and demographic characteristics with respect to postoperative National Institutes of Health Stroke Scale (*NIHSS*) score variation[a]

Variable	*NIHSS score decrease Mean ± SD*	*95% CI*	t-*test*	P
Age <70 years	4.81 ± 3.19	5.82-3.79	0.53	.60
Age ≥70 years	4.47 ± 2.63	5.23-3.71		
Male	4.65 ± 2.99	5.32-3.98	0.39	.70
Hypertension	4.66 ± 2.82	5.35-3.97	0.43	.66
Diabetes	4.38 ± 3.10	5.43-3.33	0.49	.62
Hyperlipemia	3.81 ± 3.16	4.90-2.71	1.71	.09
Smoke	5.18 ± 3.10	5.94-4.41	2.37	.02
Coronary artery disease[b]	4.64 ± 2.97	5.71-3.57	0.11	.91
Brain infarction on admission	4.26 ± 3.22	5.05-3.47	1.29	.20
CEA ≤6 hours	4.39 ± 3.35	5.40-3.37	0.50	.62
NIHSS score				
4-7 on admission	3.64 ± 1.83	4.32-2.95	4.66	.0001
≥8	6.29 ± 3.47	7.20-5.38		
ICA stenosis				
50%-69%	4.33 ± 3.37	5.31-3.35	0.66	.51
Stenosis ≥70%	4.75 ± 2.46	5.53-3.97		
Plaque composition				
Hyperechoic	4.38 ± 3.10	5.43-3.33	0.49	.62
Hypoanechoic	4.70 ± 2.71	5.45-3.95		

CEA, Carotid endarterectomy; *CI,* confidence interval; *ICA,* internal carotid artery.

[a]Continuous values analysis by *t*-test.

[b]Myocardial infarction, angina, congestive heart failure, valvular heart disease.

Primary perioperative (30-day) outcome measures were neurologic mortality; significant NIHSS score improvement or worsening, defined as a variation ≥4 at postoperative day 30; and hemorrhagic or ischemic neurologic recurrence.[12] Neurologic recurrence was defined as a new ischemic event or a significant worsening of the previous NIHSS score ≥4 lasting >24 hours.[12]

Patients were divided for analysis into subgroups according to perioperative characteristics and were compared with respect to the occurrence of postoperative neurologic events or significant NIHSS score variation (≥4). Univariate analysis was performed by *t*-test for continuous variables, and results are expressed as mean ± standard deviation (SD), and the χ^2 and Fisher's exact (one-sided) tests were used for categoric values and are expressed as numbers and percentages. A value of $P < .05$ was considered statistically significant.

RESULTS

Mean age of the entire population was 68 ± 10 years (range, 51-90 years), and 51 (82.2%) were men. Hypertension was discovered in 49 patients (79%), diabetes in 21 (33.8%), hyperlipemia in 19 (30.6%), coronary artery disease in 20 (32.2%), and smoking history in 37 (59.6%). Stenosis percentage ranged from 50% to 69% in 22 patients (35.5%) and was ≥70% in 40 (64.5%). Plaque composition was hypoanechoic in 47 patients (75.8%) and hyperechoic in 15 (24.2%) at the preoperative ultrasound evaluation.

At admission, 40 patients (64.5%) presented a mean NIHSS score of 4.95 ± 1.03 (range, 4-7; mild neurologic impairment), and 22 (35.5%) had a score of 10.32 ± 1.94 (≥8 is moderate neurologic impairment). Among those, 5 patients presented a score of 8, 16 had a score between 9 and 14, and 1 patient presented a score of 15.

The first CT or MRI scans showed an acute brain infarction in 36 patients (58%). The brain infarctions were a mean diameter of 1.2 cm (range, 0-2.1 cm). The overall mean time from neurologic event to surgery was 34.2 ± 50.2 hours (median, 31.4 hours). CEA was performed in 22 patients (35.4%) ≤6 hours from neurologic event and in 40 (64.5%) >6 hours. Among them, 12 underwent surgery ≥48 hours from onset of symptoms. The mean length of postoperative in-hospital stay was 3.3 ± 1.26 days in the entire group.

Perioperative (30-day) neurologic outcomes. No neurologic mortality, hemorrhagic brain infarction, or significant ischemic recurrence (NIHSS worsening ≥4 points) was recorded. One patient (1.6%) died of myocardial infarction on postoperative day 2.

The mean NIHSS score was 7.05 ± 3.41 on admission and 3.11 ± 3.62 at discharge in the entire group ($P < .01$). This NIHSS score decrease was observed in all but four patients (93.5%). A score increase of 3 points was detected postoperatively in one patient whose preoperative score was 8 and of 2 points in two patients whose preoperative scores were 5 and 6. In one patient, the preoperative score of 6 remained stable after surgery and at the 30-day follow-up. In all of them, preoperative CT scans had shown ipsilateral ischemic lesions with perilesional edema. No new ischemic lesion was detected at postoperative CT or MRI scans, so the clinical worsening was attributed to edema enlargement. The neurologic worsening occurred in all patients in their ipsilateral motor function.

The strongest decrease in NIHSS score after CEA occurred in patients presenting with ≥8 score on admission, varying from 10.32 ± 1.94 to 4.03 ± 3.67. The difference in the mean score decrease was statistically significant when compared with that occurring in the patients whose scores were 4 to 7, whose mean score decreased from 4.95 ± 1.03 to 1.31 ± 1.7 ($P = .0001$, Tables II and III).

An NIHSS score decrease of >4 points was detected in 28 patients (45.1%). The significant score decrease was detected in 11 patients with mild neurologic impairment (27.5% of patients presenting with NIHSS score between 4 and 7) and in 17 with moderate neurologic impairment (77.2% of patients presenting with NIHSS score ≥8; $P < .0001$).

Clinical and demographic characteristics (age, sex, hypertension, diabetes, hyperlipemia, smoke, coronary artery disease, internal carotid artery stenosis percentage, plaque composition) presented no significant relationship when analyzed with respect to their effect on NIHSS score decrease both in continuous and categoric data analysis (Figs 1 and 2, Tables II and III).

Analysis of the NIHSS score with respect to time from onset of symptoms to intervention showed no differences

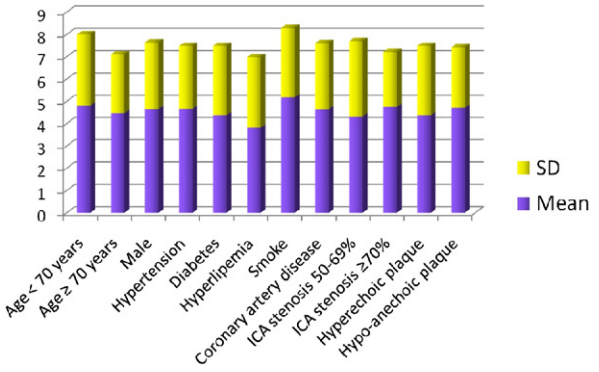

Fig 1. The postoperative National Institutes of Health Stroke Scale score decrease in stroke patients was analyzed with respect to clinical and demographic characteristics. Continuous values expressed as mean and standard deviation (*SD*).

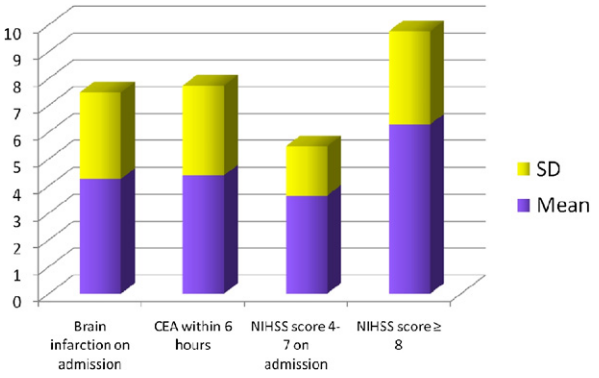

Fig 2. The postoperative National Institutes of Health Stroke Scale score decrease in stroke patients was analyzed with respect to clinical and demographic characteristics. Continuous values are expressed as the mean and standard deviation (*SD*).

in the group operated on ≤6 hours compared with patients who underwent CEA >6 hours from the onset of symptoms (10 and 18 patients, respectively, $P = .60$).

Analysis of the NIHSS score with respect to the presence of brain infarction on admission showed no statistically significant differences, given a significant (≥4) NIHSS score decrease in 16 patients (44.4%) with brain infarction on admission and 12 patients (46.1%) with no brain infarction ($P = .20$). Results of the analysis are summarized in Figs 1 and 2 and in Tables II and III.

DISCUSSION

Nowadays, CEA is considered a safe and effective intervention to prevent ischemic stroke in patients with moderate or severe symptomatic carotid artery stenosis.[13,14] In experienced centers, neurologic mortality and morbidity rates after CEA of up to 8.4% are usually reported in recently symptomatic patients with severe carotid stenosis.[15,16] In the present series, we detected no neurologic mortality in a subset of patients at high risk of intraoperative stroke event because of the short interval between the neurologic event and surgery and a strict treatment protocol.

Risk of recurrence. It is a common opinion that intraoperative stroke risk is very high in very recently symptomatic patients.[16] Recent studies have shown symptomatic plaques characteristically show features on ultrasound imaging and histology that justify their instability and their tendency to embolize.[17-19] Such unstable features are responsible for the high risk of recurrence in symptomatic patients more than previously considered. The old assumption that the early risk of stroke after a transient ischemic attack (TIA) or minor stroke was only about 1% to 2% at 7 days and 2% to 4% at 30 days was derived from a collection of cohort studies biased in design.[20-23] Those studies were inclined to recruit patients some time after the neurologic event, excluding those who sustained a stroke in the intervening period. Conversely, a meta-analysis of recent studies[24] published in 2007 observed that the risk of stroke was 6.7% at 2 days and 10.4% at 7 days, thus reporting much higher values than previously accepted.

In a review of data on 2416 patients who had presented with an ischemic stroke, Rothwell et al[25] observed that approximately one-quarter of patients reported a preceding TIA, with 17% of those occurring at the same day of stroke, 9% happening on the day before the stroke, and 43% of overall TIAs occurring ≤7 days before stroke onset. Lovett, et al[23] reported that stroke due to "large artery" disease (ie, predominantly involving the carotid artery) was associated with the highest rate of early recurrent stroke (4% at 7 days, 12.6% at 30 days, 19.2% at 3 months). In a recent observational study, Ois et al[26] recorded a neurologic recurrence of 20.9% within 72 hours, 6.7% between 72 hours and 7 days, and 3.7% at 14 days in 163 patients with symptomatic carotid stenosis and initial mild stroke or TIA.

In this context, the National Institute for Clinical Excellence recommendation that all patients should be treated ≤2 weeks of onset of symptoms[27] has been superseded by the United Kingdom Department of Health recommendation that carotid intervention should be regarded as an emergency procedure in stable symptomatic patients and should ideally be performed ≤48 hours of a TIA or minor stroke.[28] In the present series, the mean time from the index event and surgery was 34.2 ± 50.2 hours, with about one-third of patients operated on ≤6 hours of symptoms onset, thus partially justifying the absence of recurrences reported or detected by postoperative CT or MRI scans.

Risk of hemorrhagic transformation of brain infarct. If any intervention delay rapidly diminishes the benefit accruing to the patient in stroke prevention,[16] nevertheless, the risk of hemorrhagic transformation of the ischemic area is a cause of major concern. Bond et al[29] systematically reviewed the 30-day risk of stroke/death in 4278 patients presenting with a minor stroke who underwent early CEA (<3 to 6 weeks) vs late CEA (>3 to 6 weeks) and demonstrated that no excess risk was associated with early vs late CEA, provided the patient presented with stable neurologic symptoms.

A literature review of 30-day outcomes and conversion rates to intracranial hemorrhage in eight studies published from 2000 to 2007, where the median delay from onset of events to surgery was <14 days,[16] concluded that the overall 30-day death/stroke rates probably were higher than those cited in the "popular" literature, whereas the 16.4% risk was probably not typical of the type of patient normally being considered for early intervention. The rate of conversion to intracranial hemorrhage was reassuringly low, ranging from 0% to 4%, with the highest value encountered in a series of patients with positive CT scans not associated with symptoms.

Following previous reports by our group[8,9] and according to the literature review,[16] a strict selection protocol could help identify those patients who could most benefit from very early CEA and, above all, who should avoid early surgery, given the high risk of recurrence and hemorrhagic transformation. In the present series, the application of those inclusion and exclusion criteria (see Table I) allowed us to avoid any significant worsening of neurologic status. In those patients not presenting an NIHSS score decrease, no new ischemic lesion was detected at postoperative CT or MRI scans, so that the worsening was attributed to perilesional brain edema. Conversely, an improved NIHSS score was detected after surgery in 93.5% of patients, with the highest decrease recorded in those patients presenting with moderate neurologic impairment.

Brain tissue rescue. Apart from preventing ongoing embolism or carotid thrombosis, the early CEA could improve overall cerebral perfusion, restoring blood flow to the ischemic penumbra and thus reducing neuronal loss. Blood flow in the ischemic penumbra is far from normal, but at the same time is not absent, so the hypoperfused tissue can be still considered at risk for infarction but not openly ischemic. In diffusion-weighted MRI, that area is detected as a "mismatch" between perfusion and diffusion scans.[30,31] Expeditious blood flow restoration to that area, which is exponentially larger depending on the diameter of the ischemic area, could help in preventing progressive flow reduction caused by perilesional edema. The same principle governs thrombolytic therapy in acute cerebral arteries occlusion, where rt-PA could be used ≤3 hours from the event, with recovery of hypoperfused brain areas and clinical status improvement.[10]

The main limitation of the present study is the small number of patients. We report a single-center experience with very early CEA in symptomatic patients. Although they cannot be representative of the entire population, nevertheless, the results follow those reported in a multicenter experience gained in Italy[8,9] that shared the same treatment protocol.

In most cases, the short interval between observation and surgery has not allowed us to properly classify patients presenting with a stroke or a TIA. Nevertheless all patients in the present series presented a neurologic impairment (NIHSS score ≥4) at time of CEA.

When analyzing results, we divided patients with respect to <6 hours or >6 hours from onset of symptoms to intervention. This time was chosen assuming that the flow in the ischemic penumbra was close to zero. The survival time of neuronal cells and the consequent ability to recover in case of ischemia are very short. In an emergency situation, it is quite impossible to know exactly the blood flow in the ischemic penumbra, so the shortening of time from neurologic event and intervention is mandatory.

CONCLUSIONS

Early CEA has proven to be effective in preventing neurologic recurrence in symptomatic patients and is able to guarantee a low risk of hemorrhagic conversion applying a proper treatment protocol. If the previous aim of urgent CEA is to prevent neurologic recurrence, the new and challenging goal is to rescue substantial brain tissue as soon as possible. Close collaboration among neurologists, neuroradiologists, and vascular surgeons is mandatory to select patients who could most benefit from urgent carotid revascularization.

AUTHOR CONTRIBUTIONS

Conception and design: LC, ES, FS, DT, PF
Analysis and interpretation: LC, DT
Data collection: ES
Writing the article: LC
Critical revision of the article: ES, FS
Final approval of the article: FS, PF
Statistical analysis: LC
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Overall responsibility: FS

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DISCUSSION

Dr Ali AbuRahma (*Charleston, WV*). There is no doubt that we tend to do procedures much earlier now than we did 20 to 30 years ago, but since the patients in your study were nonrandomized, how do you know that the change didn't just occur on its own?

Dr Laura Capoccia. Thank you for your question. Of course, I can't derive evidence from such a small number of patients, and sure enough, when looking at neurologic improvement, I have to consider not only the procedure itself but, for example, heparin administration or blood pressure control during the procedure. I can't be 100% sure that we don't have other factors affecting our results. I am just reporting what our results are. And those are that the major part of our patients are improving neurologic outcome. Of course, this is not direct evidence, this is indirect evidence; nevertheless, it seems to relate to the brain tissue rescue.

Dr John Ricotta (*Washington, DC*). Could you tell us a little bit more about medical efforts at plaque stabilization, antiplatelet, heparin, statin use in your patients, and use of a shunt during surgery. Do you routinely shunt these patients during surgery? Can you comment on the alternative strategy of trying to stabilize these patients for 3 or 4 days on medical therapy rather than moving immediately to surgery?

Dr Capoccia. Regarding the second comment or question, our treatment protocol is to operate on stable patients as soon as possible, provided that the inclusion criteria are met. We think this is the best strategy in order to minimize the recurrence risk and to save the brain tissue. By the way, in this group of patients, all patients were stable patients because the unstable ones were excluded from the analysis.

And to answer the first question, we don't use routinely a shunt. We generally use transcranial Doppler (TCD) monitoring of patients, or if not possible, we have the near-infrared spectroscopy (NIRS) monitoring. When we have evidence that the blood flow to the brain is not enough, we use a shunt. In this group, 13 patients were submitted to carotid endarterectomy by use of a shunt. Regarding therapy, all patients received their scheduled antihypertensive, antiplatelet, and statin therapy in the postoperative period together with 4000 to 6000 IU of low-molecular-weight-heparin.

Dr Ahmed Taha (*Cairo, Egypt*). How could you explain the 0% incidence of reperfusion injury and hemorrhagic infarction in your series? Is there any special protocol you followed in order to nullify these complications, especially when the time between the stroke and surgery is that short?

Dr Capoccia. I am aware those were excellent results. I think the main point of our study is the accuracy of the protocol with respect to inclusion and exclusion criteria. This protocol allowed us to include only patients who could really benefit from urgent carotid endarterectomy CEA, thus excluding those at risk of having a worsening of neurological status.

Dr R. Clement Darling (*Albany, NY*). We have done >300 CEAs in acute stroke, and we have actually changed some of our approaches. We do it with eversion endarterectomy. We tend to shunt these more aggressively, and we tend to do them under general anesthesia, when we do 99% of our electives under cervical block. How do you monitor their cerebral activity during your operation? And do you do them under general or under block?

Dr Capoccia. We performed all with general anesthesia in those patients. Our cerebral activity monitoring was by transcranial Doppler whenever possible, and NIRS monitoring in all patients.

Dr Richard Cambria (*Boston, Mass*). This is a clinical decision-making issue that is a common problem for vascular surgeons. You reported on 62 patients that you treated, and I think most of us would agree that many of the patients that you excluded are patients that we would not operate on urgently. Can you tell us the content of the whole series, in other words, how many exclusions did you have in your cohort?

Dr Capoccia. I don't remember the exact number, but the whole cohort was around 110. They were all patients admitted with a neurologic event and an ipsilateral carotid stenosis of >50%. So I can say about half of the patients admitted with a carotid-related stroke could be submitted to urgent CEA.

Dr Wilhelm Sandmann (*Düsseldorf, Germany*). Thank you for your paper. It shows the persistence of Paolo Fiorani, who always stated that urgent endarterectomy is possible. But can you tell us how many occlusions you have found at the time of surgery? Because sometimes if it is an urgent case, you go ahead maybe also without imaging, and when you open the carotid artery up it is already occluded. Did this happen in your series also?

Dr Capoccia. We treated patients with recently occluded carotid artery, but they were not analyzed in this series. We excluded from this analysis patients presenting with thrombus in the carotid artery or occlusion, because, of course, they were unstable patients in our experience. Indeed, they were all patients with a patent carotid artery on admission and an occluded one in the operating room, so all of them presented unstable or fluctuating symptoms and were excluded from the present analysis.

INVITED COMMENTARY

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This article will polarize opinion, depending on whether one believes that symptomatic patients should be treated as emergencies. Consequently, and notwithstanding the excellent results by Capoccia et al, some surgeons will remain concerned that the small numbers (12 patients per annum) mean that this series is too selective to permit meaningful interpretation, given that others have reported significant increases in procedural risks where carotid endarterectomy (CEA) was performed more urgently.[1] In the currently litigious era, is it any wonder that some surgeons might encourage delays to minimize the procedural risk? By contrast, those aware of the very high natural history risk of stroke in the first 72 hours after a transient ischemic attack (TIA) or minor stroke will be pleased that evidence is now emerging that CEA can be performed with relatively low risks in selected patients within the hyperacute period.

So how should these data be interpreted? To me, the first issue is the definition of procedural stroke. I remain uncertain why stroke was defined as being a deterioration of ≥4 points on the National Institutes of Health Stroke Scale (NIHSS) score. In the study by Capoccia et al, three patients increased their postoperative NIHSS score by 2 or 3. In many units, these would be classified as minor strokes leading to a death/stroke rate of 6.5% as opposed to the 1.6% cited. But is a 6.5% risk too high? To this observer, the answer is "no," and this is crucial to changing attitudes about whether early intervention increases the procedural risk to the extent that it might negate any long-term benefit. Paradoxically, meta-analyses suggest that the surgeon who operates early with a 10% risk may still prevent more strokes than the surgeon who waits >4 weeks and then operates with a 0% risk.[2]

The second issue is to explain the drive toward emergency intervention in Europe. Previously, we were taught that the 7-day risk of stroke after TIA was 2%. However, contemporary studies suggest that this value may be nearer 10%,[3] while others have reported that almost half of all strokes occurring ≤7 days do so within the first 24 hours.[4] Of concern to the vascular surgeon should be a recent Canadian study which showed that TIA patients with a 50% to 99% stenosis faced a 17% risk of recurrent stroke at 72 hours, 22% at 7 days, and 25% at 14 days.[5] Those who retort that they never see such a high a rate of recurrent stroke on their CEA waiting lists should be aware that most of these strokes will have occurred long before they ever had a chance to see the patient in the first place!

For too long, TIA has been the poor relation of heart disease, and the time has now come for it to be treated on par with acute myocardial infarction. However, this will require guideline makers to recognize that surgeons who delay interventions so they can offer the lowest procedural risk may look good in league tables without conferring much benefit to their patients!

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